NICHOLAS SCHOOL OF THE ENVIRONMENT AND EARTH SCIENCES
DUKE UNIVERSITY

CHILDREN'S ENVIRONMENTAL HEALTH INITIATIVE
Marie Lynn Miranda, PhD • Director

July 2, 2007

Nigel A. Fields
Project Officer/Environmental Health Specialist
US Environmental Protection Agency
National Center for Environmental Research

Dear Nigel,

Dr. Miranda requested that I send this to you after receiving Marcy Speer's signature. Dr. Speer was out of the country so we had to wait to send you the hard copy of the QMP. Dr. Miranda is currently on holiday.

Thank you so much for your assistance with this project. We look forward to continued conversations.

Sincerely,

(b) (6) [redacted]

Pamela J. Maxson
Project Manager/ Quality Assurance Manager
SCEDDBO
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Nigel Fields/DC/USEPA/US
07/23/2007 12:12 PM

To pamela.maxson@duke.edu
cc mmiranda@duke.edu
bcc
Subject SCEDDBO QMP

Hello Dr. Maxson,

I've signed and approved the SCEDDBO QMP. A pdf of the two signature pages are attached. However I am requesting further information regarding Sections 2 and 4 of the QMP. You may submit your responses via email.

Section 2: Can you please say more regarding the systematic auditing approach for the Center. Also please explain when and how corrective action will be implemented.
Section 4: Can you please explain SCEDDBO's approach for data preservation.

Kind Regards,

Nigel Fields
202.343.9767

SCEDDBO_QMP_Signed_23July07.pdf

DUKE QMP FINAL

Southern Center for Environmentally Driven Disparities in Birth Outcomes Comprehensive Quality Management Plan

Approved by:

(b) (6)

22 June 2007

Marie Lynn Miranda, Ph.D.
The Nicholas School of the Environment and Earth Sciences
Director, Children's Environmental Health Initiative
Principal Investigator and Center Director
Leader, Research Project A

(b) (6)

22 June 2007

Sherman James, Ph.D.
Susan Bennett King Professor of Public Policy Studies
Terry Sanford Institute of Public Policy
Center Co-Director

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29 June 2007

Marcy Speer, Ph.D.
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and Biostatistics and Bioinformatics
Center Co-Director

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22 June 2007

Redford B. Williams, Jr., M.D.
Psychiatry and Behavioral Sciences
Director of the Duke University Medical Center's Behavioral Medicine Research Center
Leader, Research Project B

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22 June 2007

Richard L. Auten, M.D.
Duke University Medical Center Department of Pediatrics and Neonatology
Leader, Research Project C

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26 June 2007

Alan E. Gelfand, Ph.D.
mes B. Duke Professor of Statistics and Decision Sciences
eader, GISSA Core

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Pamela Maxson, Ph.D.
Research Associate, Children's Environmental Health Initiative
Project Manager and Quality Assurance Manager

28 June 2007
Date

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Nigel A. Fields
Project Officer /Environmental Health Scientist
US Environmental Protection Agency
National Center for Environmental Research

23 July 2007
Date

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1 Management and Organization

1.1 Organizational Policy on Quality Assurance

The Southern Center on Environmentally Driven Disparities in Birth Outcomes (SCEDDBO) is strongly committed to utilizing quality management (QM) practices in order to conduct good science. We view a comprehensive and integrated QM program as critical to accomplishing the scientific objectives of the center, including providing EPA with research insights that are based on scientifically sound and well-documented research practices. We have developed integrated quality management practices for center data collection, analysis, and modeling stages. This Quality Management Plan (QMP) summarizes the Quality Assurance (QA) structure of SCEDDBO and identifies the quality control responsibilities of all researchers operating through the Center. The SCEDDBO QM program will be administered by the SCEDDBO Project and QA manager, Dr. Pamela Maxson, who will report directly to Dr. Marie Lynn Miranda, the Center Principal Investigator and Director.

Per Nigel Fields and section 1.2, paragraph 3, of *EPA Requirements for Quality Management Plans, EPA QA/R-2*, this comprehensive document combines the individual Quality Assurance Project Plans (QAPPs) and the QMP into a "single document that contains both organizational and project-specific elements." Thus we refer to this document as our Comprehensive QMP.

Each of the Principal Investigators of the three research projects (A, B, and C) that compose the SCEDDBO research program will be responsible for overseeing the quality assurance efforts associated with their projects. In addition, Dr. Maxson will provide regular oversight and guidance on QA procedures for all components of the Center.

1.2 Organization

The Center includes an Administrative Core; three Research Projects (Research Project A: Mapping Disparities in Birth Outcomes; Research Project B: Healthy Pregnancy, Healthy Baby: Studying Racial Disparities in Birth Outcomes; and Research Project C: Perinatal Environmental Exposure Disparity and Neonatal Respiratory Health); one Facility Core (Geographic Information System and Statistical Analysis – GISSA – Core); and a Community Outreach and Translation Core (COTC). **Figure 1** provides an organizational chart for SCEDDBO, including designations of key contact people within each component who are responsible for liaising with QA Manager Pamela Maxson to ensure that all QM practices are followed.

SCEDDBO organizational management includes an Executive Committee consisting of the Center Director, the two Center Co-directors, and the Project Manager. This group meets at least monthly and additionally on an as-needed basis. Some work of the work is conducted via email.

SCEDDBO also benefits from an Internal Steering Committee, consisting of the Executive Committee, as well as the Principal Investigators from the three research projects, and the Directors of the GISSA Core and the Community Outreach and Translation Core.

SCEDDBO also relies on a Science Advisory Committee to assist in evaluating the scientific progress of the Center, the relative success of each of the functional units of the Center, the ability of the program to enhance the function of its individual components, the progress in

achieving collaboration and synergy among Center investigators, and the degree to which the center successfully partners with the community. The Science Advisory Committee consists of representatives from academia, industry, environmental organizations, and governmental entities, and also includes the EPA SCEDDBO Project Officer, Nigel Fields.

Figure 1.

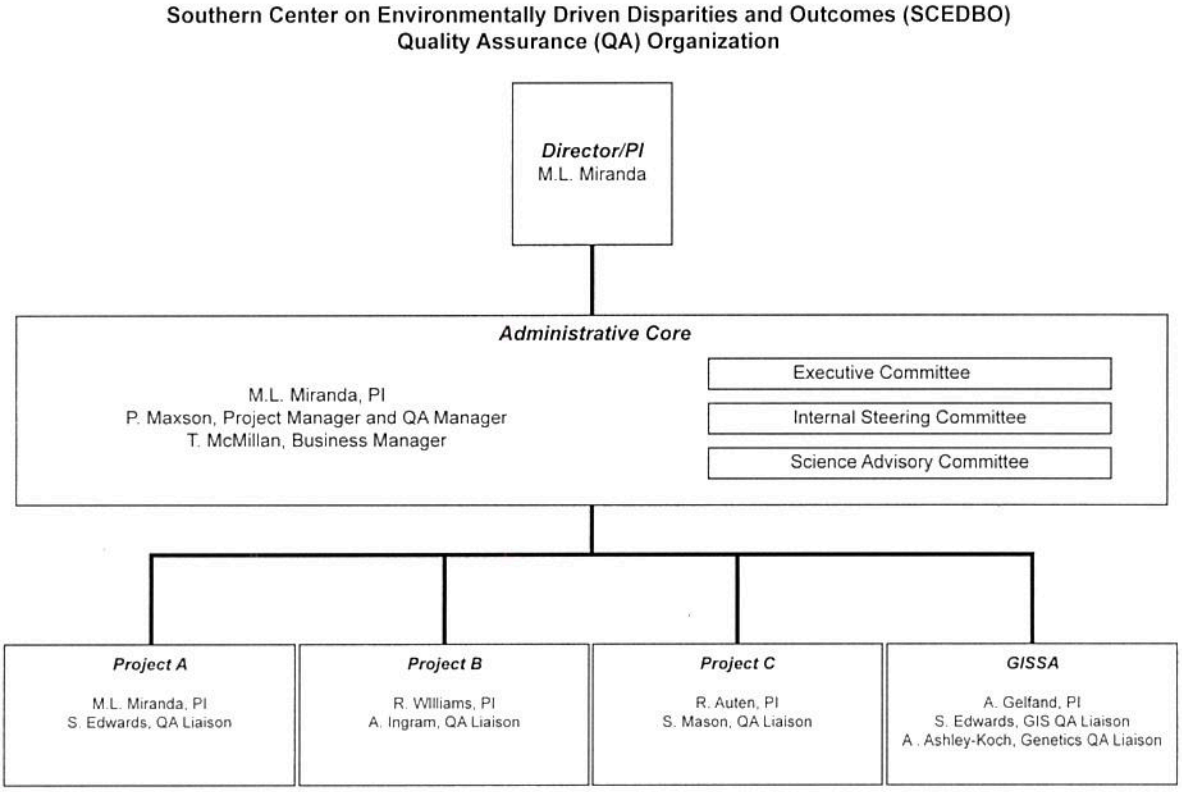

Figure 1. SCEDDBO Quality Assurance Organization

1.3 Authorities of the QA Manager and QA Staff

Dr. Marie Lynn Miranda, the Center Director, will have ultimate responsibility for quality management throughout SCEDDBO. Dr. Miranda will work closely with Dr. Maxson to ensure that QA approaches are observed throughout daily operations across all center components. The Principal Investigator for each project has assigned a liaison who will work directly with the QA manager, Dr. Maxson. This person will be responsible for reporting to Dr. Maxson as well as bringing all questions regarding QA practices to her. Dr. Maxson will be in regular direct contact with the liaison from each project.

The PI in charge of each Research Project or Facility Core will be responsible for implementing the quality management plan for their respective project. The QA manager, the Principal Investigators, and the liaisons from each project will work together to ensure diligence in Quality Assurance practices.

All significant QA issues and concerns will be raised and discussed at monthly Executive Committee meetings and, if necessary, Internal Steering Committee meetings. The resolutions of these issues will then be discussed with the liaison from each project.

The SCEDDBO Science Advisory Committee will be provided a Quality Assurance update and consulted as appropriate.

1.4 Project Management and Technical Activities Supported by the Quality System

The SCEDDBO quality system will support the center overall, but will be especially directed toward four center components:

- Research Project A: Mapping Disparities in Birth Outcomes
- Research Project B: Healthy Pregnancy, Healthy Baby: Studying Racial Disparities in Birth Outcomes
- Research Project C: Perinatal Environmental Exposure Disparity and Neonatal Respiratory Health
- Geographic Information System and Statistical Analysis Facility Core

Below we provide an overview on the center as a whole as well as the four constituent parts governed by this Comprehensive QMP.

1.4.1 Center Overview

The **central mission** of the **Southern Center for Environmentally-Driven Disparities in Birth Outcomes is to determine how environmental, social, and host factors jointly contribute to health disparities.** Specific aims of the Center are:

1. To develop and operate an interdisciplinary children's health research center with a focus on understanding how biological, physiological, environmental, and social aspects of vulnerability contribute to health disparities;
2. To enhance research in children's health at Duke by promoting research interactions among programs in biomedicine, pediatric and obstetric care, environmental health, and the social sciences and establishing an infrastructure to support and extend interdisciplinary research;
3. To develop new methodologies for incorporating innovative statistical analysis into children's environmental health research and policy practice, with a particular emphasis on spatial, genetic and proteomic analysis;
4. To serve as a technical and educational resource to the local community, region, the nation, and to international agencies in the area of children's health and health disparities; and,
5. To translate the results of the Center into direct interventions in clinical care and practice.

Dr. Marie Lynn Miranda serves as PI/Director of SCEDDBO, and Drs. Sherman James and Marcy Speer serve as Co-Directors. Their expertise in spatial analytics, social epidemiology, and genetics, respectively, provides a strong basis for QA throughout the integrated components of SCEDDBO. Dr. Pamela Maxson serves as the SCEDDBO QA manager.

1.4.2 Research Project A: Mapping Disparities in Birth Outcomes

The **central objective** of **Research Project A is to determine whether and to what extent joint exposures to environmental and social stressors contribute to racial and ethnic disparities in fetal growth restriction.** The organizing framework for the project is the "weathering hypothesis," an approach that posits that chronic and persistent stressors lead to *accelerated biological aging* of women, which in turn accounts for excess infant mortality and adverse pregnancy outcomes among certain subpopulations. Using a geographically-based nested study design and high-end Geographic Information Systems (GIS) applications in combination with Bayesian spatial hierarchical modeling and other advanced spatial statistical approaches, the **specific aims** are to:

1. Spatially link detailed birth record, fetal death certificate, socioeconomic, environmental exposure, tax assessor, community-based, and clinical obstetric data at highly resolved scales for the State of North Carolina from 1990-2003.
2. Refine the conception of fetal growth restriction by:
    a. Developing a joint distribution for birthweight and gestation using bivariate modeling for live births and fetal deaths – both separately and jointly.
    b. Defining it in terms of fetal and infant mortality, rather than percentile cut points.
3. Determine whether and to what extent differential exposures to both socioeconomic and environmental stressors help explain health disparities in fetal growth restriction among:
    a. African-American women compared to Non-Hispanic whites and Hispanic women.
    b. Older African-American women compared to younger African-American women.
    c. Hispanic women compared to Non-Hispanic whites and African-American women.
    d. Foreign born Hispanic women compared to United States born Hispanic women.

Dr. Marie Lynn Miranda serves as the Principal Investigator on this project, with Dr. Sherman James as Co-Principal Investigator. Ms. Sharon Edwards serves as the QA liaison on Research Project A.

1.4.3 Research Project B: Healthy Pregnancy, Healthy Baby: Studying Racial Disparities in Birth Outcomes

The **central objective** of this project is **to explain racial disparities in birth outcomes by determining how the interaction among host, social, and environmental factors shapes birth outcomes between and among African-American and white mothers in the American South**. To this end, our specific aims are to:

1. Conduct a cohort study of pregnant women in Durham, NC designed to correlate birthweight, gestational age, and birthweight x gestational age with individual-level measures of key environmental, social, and host factors including:
    a. Measuring exposures to heavy metals and environmental tobacco smoke;
    b. Evaluating social factors using standardized modules of stress and behavior; and,

c. Assessing personality, genetic, age, co-morbidity, and biological response host factors.

2. Develop community-level measures of environmental and social factors by inventorying neighborhood quality and the built environment in partnership with local community groups.
3. Create a comprehensive data architecture, spatially resolved at the tax parcel level, of environmental, social, and host factors affecting pregnant women by linking data from the cohort study and neighborhood assessments with additional environmental and socioeconomic data,
4. Determine whether and to what extent differential exposures explain health disparities by applying innovative spatial and genetic statistical methods to:
    a. Identify environmental, social, and host factors that cluster to predict birth outcomes in the entire sample;
    b. Determine whether the clusters in (4a) are more or less present in African-American versus white populations and quantify the proportion of health disparities explained by differences in cluster frequency; and,
    c. Identify environmental, social, and host factors that cluster to best predict birth outcomes within the African-American and white sub-samples and compare these clusters across racial groups.

Dr. Redford Williams serves as Principal Investigator on this project, with Dr. Alison Ashley-Koch leading the efforts on genetic analysis, and Dr. Geeta Swamy directing the clinical components of the study. Ms. Amber Ingram serves as the QA liaison on Research Project B.

1.4.4 Research Project C: Perinatal Environmental Exposure Disparity and Neonatal Respiratory Health

The **central objective of Research Project C is to determine whether prenatal air pollution exposure provokes maternal/fetal humoral responses that impair fetal and postnatal growth and lung development, leading to impaired lung function in a perinatal mouse model of exposure.** The project posits that maternal exposure to single versus combined airborne environmental pollutants (particulate matter and ozone) contributes to direct effects on fetal lung development and indirect effects through growth restriction that impairs fetal growth and development. This represents a "first hit." Inflammation is strongly implicated as a mechanistic link. Postnatal ozone exposure is a "second hit" that leads to abnormal airway development. Resulting smooth muscle hyperplasia/hypertrophy, airways hyperreactivity, and epithelial mucus metaplasia contribute to impaired mechanics. Inflammation is a central mechanistic link between exposure and altered lung mechanics by which genetic or developmental susceptibility (e.g., changes in cell-mediated immunity) exaggerates the disparity in health effects. To this end, our specific aims are:

1. To determine whether maternal exposure to airborne particulates (PM) and/or ozone (1st hit) restricts fetal growth and/or postnatal growth, and impairs lung development/function in newborn mice;
2. To determine whether PM and/or ozone exposure 're-programs' maternal inflammatory responses;

3. To determine whether postnatal (2nd hit) ozone exposure further impairs postnatal somatic and lung development/function following maternal PM and/or ozone exposures;
4. To determine whether genetic or developmental susceptibility to airway hyperreactivity exacerbates maternal and/or postnatal exposure effects on postnatal somatic and lung development/function.

Dr. Richard Auten serves as Principal Investigator on this project, with Dr. W. Michael Foster leading the efforts on exposure delivery. Mr. Stanley N. Mason serves as the QA liaison on Research Project C.

1.4.5 Geographic Information System and Statistical Analysis Facility Core

The overall objective of the GIS and Statistical Analysis Core is to **support spatial and quantitative analysis needs of the Center research projects, as well as the Community Outreach and Translation Core.** Our specific aims include:

1. To provide support for the development of environmental and social data layers needed to implement the various data analyses required for the research projects and the Community Outreach and Translation Core;
2. To provide statistical analysis, advice and consulting on the broad range of statistical issues which arise in conjunction with the research projects, with a particular emphasis on data reduction methods and modeling spatial and spatio-temporal data within a Bayesian framework; and,
3. To provide analysis for the unique needs of genetic data arising from the clinical and animal studies of the center.

Dr. Alan Gelfand serves as Principal Investigator on this facility core, with Dr. Allison Ashley-Koch leading the efforts on genetic analysis and Dr. Marie Lynn Miranda leading the efforts on spatial data architecture. Ms. Sharon Edwards serves as the QA liaison for spatial analysis and Dr. Allison Ashley-Koch serves as the liaison for genetic analysis within the GISSA Core.

1.5 Assuring QA System is Understood and Implemented

Meetings with Center personnel will facilitate understanding and successful implementation of the QA system. Center Principal Investigators, along with relevant key study personnel, attend monthly center meetings. These meetings are established to plan and/or discuss progress on each research project, evaluate how any recent publications or findings affect the proposed research, and collaborate on redesign or expansion of research activities to make best use of these findings. All issues pertaining to QA and associated response actions will be discussed at these meetings. The SCEDDBO investigators have developed an effective system of communication across disciplines and in the face of rapidly developing research.

Continual communication between the QA Manager and the individual projects will assure understanding and implementation of quality system practices. Dr. Pamela Maxson, the QA Manager, will be available for consultation at all times to all project Principal Investigators as well as Center staff regarding QA questions.

Liaison people from each individual project will be responsible for directing questions and concerns to Dr. Maxson who will then respond to the questions/concerns. Regular communication will ensure that all questions are raised in a timely manner.

1.6 Dispute Resolution Process

In the event of a dispute relevant to Quality Assurance, the initial step will be consultation with Quality Assurance Manager, Dr. Maxson. If this interaction is not sufficient, a meeting will be held with the Executive Committee, the individuals involved in the dispute, and the liaison from the relevant project. The goal of this meeting would be to resolve the issue. In the event that the issue is not resolved through these steps, SCEDDBO Principal Investigator/Director, Dr. Marie Lynn Miranda, will make the final decision regarding the dispute.

The well-established and healthy communication patterns and overall research relationships among all staff involved with SCEDDBO will help to assure that problems are resolved long before they would be elevated to a dispute resolution process.

2 Quality System Components

2.1 Description of Quality System

Quality system documentation, including the Comprehensive Quality Management Plan, annual reviews and plans, and training protocols, will be maintained by Dr. Pamela Maxson, SCEDDBO Project Manager and QA Manager. Production of these documents will be coordinated by Dr. Marie Lynn Miranda, Center Principal Investigator/Director. Individual project Principal Investigators will create and maintain relevant training documents.

2.2 Quality System Implementation Tools

- **Comprehensive Quality Management Plan**: We are submitting an integrated Comprehensive QMP that covers the QMP and QAPP components in a single document.
- **Training protocols**: Protocols for training new staff for each of the research projects and for the GISSA Core will be established and implemented by the Principal Investigator of each center component. Any updates on training protocols will be summarized and communicated during the monthly center meetings.
- **Data audit documents**: Documentation of all data audits will be centrally maintained by Dr. Pamela Maxson, SCEDDBO QA Manager.

2.3 Development of QM Plans

This Comprehensive QMP has been jointly developed by the Principal Investigators of each research project and the GISSA Core, as well as the Center Director, Co-Directors, and QA Manager. In signing the cover sheet of this Comprehensive QMP, all signatories indicate their commitment to abide by the QA procedures laid out in this document. Drs. Maxson and Miranda will be responsible for quarterly review of the Comprehensive QMP to ensure that any needed changes are discussed during Center monthly meetings and implemented in a timely fashion.

3 Personnel Qualification and Training

3.1 Training Policy

Principal Investigators for each individual project will regularly evaluate all project staff members for key additional training requirements. This training and assessment will occur continually throughout the year, and opportunities for training will be offered as needed.

Of particular concern to SCEDDBO is training with respect to human subjects' research. Duke University's Office of Research Support maintains IRB certification and continuing education records for all University faculty and staff who work on projects dealing with human subjects. Similarly, Duke Health System's IRB Office maintains records on all medical center employees who work with human subjects.

The human subjects protocols for Research Project A is detailed in IRB protocol # 1081 (see attached). The human subjects protocols for Research Project B is detailed in IRB protocol # 7227 (see attached).

SCEDDBO is equally concerned about training with respect to use of animals in research. Research Project C uses mice as the experimental model. Project C personnel are trained in the appropriate handling and exposure of animals by the Co-investigators and the senior technician and all have completed institutionally mandated training for animal handlers required by the Institutional Animal Care and Use Committee (IUCAUC) and the Office of Animal Welfare Assurance.

The animal use protocol for Research Project C is detailed in IUCAUC protocol # A329-05-11 (see attached).

A centralized database on IRB and IUCUAC certification and continuing education requirements will be maintained by SCEDDBO Business Manager, Ms. Patricia McMillan. Twice a year, Dr. Pamela Maxson, the QA Manager, will verify that all researchers associated with SCEDDBO have completed their basic certification and continuing education (one credit of continuing education is required each year to maintain certification) requirements. Reminders will be sent to investigators when they are due for additional training. In addition, Dr. Maxson will be responsible for ensuring IRB and IUCAUC Protocols are renewed and updated as necessary. All of these documents will be posted to the SCEDDBO internal website, and paper copies will be centrally maintained by Dr. Maxson.

3.2 Ensuring Adequate Training

All SCEDDBO management and staff have been hired through competitive processes and are trained with diligence. Each individual project trains relevant personnel according to their study protocol.

3.2.1 Research Project A: Mapping Disparities in Birth Outcomes

Prior to working with any of the Detailed Birth Record data, personnel complete Human Subjects training and are familiarized with the technical solutions in place to ensure data confidentiality through an orientation to the private computer network in use by SCEDDBO. Training on using the Detailed Birth Record data involves an outline of the details of all relevant data sharing agreements, a discussion of the data documentation and various issues previously identified, and an update on the current status of data processing, including geocoding and linkages to other spatial data.

In compliance with University and IRB requirements, all personnel take annual continuing education credits to maintain their certification to work with human subjects.

3.2.2 *Research Project B: Healthy Pregnancy, Healthy Baby: Studying Racial Disparities in Birth Outcomes*

Clinical recruiters are trained through an extensive protocol involving shadowing and supervision. New recruiters follow experienced recruiters through the entire process of subject screening, approach, and consent. After a period of shadowing, new recruiters approach and consent participants with the supervision of the experienced recruiter. During this process, feedback is given to ensure consistent and correct procedure. After two weeks of intensive supervision, the new recruiter continues independently with continual contact with the trainer and the Project Manager.

This process is replicated for data entry. Training is exhaustive and extensive. A training protocol is given to relevant personnel for review. In the event of protocol changes, recruiters are thoroughly trained and updated on these changes.

In compliance with University and IRB requirements, all personnel take annual continuing education credits to maintain their certification to work with human subjects.

3.2.3 *Research Project C: Perinatal Environmental Exposure Disparity and Neonatal Respiratory Health*

Personnel are directly trained by the investigators for Project C (Drs. Auten and Foster). The senior technical personnel in the laboratories of Drs. Auten and Foster have extensive experience in the methods to be employed in Project C. Procedures are explicitly described in detailed protocols and observations recorded contemporaneously.

All personnel working with animals on Project C have been listed on the approved protocol, and have received Animal Users training provided by the Duke University Department of Laboratory Animal Resources. In addition, specific training relevant to procedures for Project C is provided by Drs. Auten and Foster.

3.2.4 *GISSA Facility Core*

All GIS and statistical staff are thoroughly trained on the mechanisms in place to protect data confidentiality. Personnel of the GISSA Core receive access to the private computer network that supports this project and are familiarized with relevant data sharing agreements. Along with an orientation to the data architecture and standards used on our servers, staff are provided with detailed metadata for all datasets.

Introductory as well as advanced training for all software packages are available to project staff. Personnel are encouraged to seek out additional educational opportunities for new software and extensions relevant to the work of the GISSA Core.

In compliance with University and IRB requirements, all personnel take annual continuing education credits to maintain their certification to work with human subjects.

4 Procurement of Items and Services

4.1 Reviewing and Approving Procurement Documents

Duke University's Office of Sponsored Programs (OSP) is responsible for monitoring compliance with regulations concerning procurement on all grants and for maintaining records of invoices. Duke University has many systems in place that assist in all aspects of procurement and property management: OSP reviews Purchase Requisitions for allowability and title; Procurement Services' purchasing system conforms with government and Duke regulations and maintains records that verify compliance; and Plant Accounting maintains inventory records and performs physical inventories for all equipment regardless of ownership.

Duke University Procurement Services (DUPS) establishes supplier relationships that consider and encourage total cost of ownership; streamlines the buy/pay process throughout the supply chain; listens and responds to changing business needs and practices; conducts business affairs in a manner that is open, competitive and fair; complies with federal requirements; monitors quality of items and services to ensure that vendors supply the highest quality goods and services; and is a dynamic, resourceful, and committed partner with the Duke community in reducing costs. Since the Center Principal Investigator (PI) and each project's Grant Manager are the most knowledgeable persons with respect to the equipment being used or needed in a sponsored project, the day-to-day responsibility of property management for property acquired or services rendered with sponsored funds remains with the PI and project grant manager. In addition, all staff members are responsible for inspecting purchased goods or services to verify that technical and quality requirements are met.

The purchase of goods or services at Duke University is facilitated via purchase requisition or via procurement card. Purchase requisitions are completed by the staff members/researchers working on the project, are approved by the Research Project PI and project grant manager, and submitted to Procurement Services for review, approval, and purchase. Purchase requisitions must be used for any purchase in excess of $1,500. The Procurement Card is a MasterCard product administered by GE Capital. The Procurement Card has been implemented to provide departments with a more efficient system for purchasing goods & services. The procurement card can be used for most purchases of goods and services up to $1,500 and for travel transactions up to $3,000. Individual procurement card purchases are reviewed and approved by the project grant manager via the PARIS system. Documentation for individual purchases made via procurement card are maintained by the project grant manager and explained appropriately within the PARIS system when approving charges/expenses. Documentation for purchases made via purchase requisition are maintained in the Department of Financial Services and at the department.

The Research Project Principal Investigator is ultimately responsible for approval of all items expensed to the sponsored project. The project grant manager handles the day to day review and approval process. Each month the project grant manager performs a detailed line item reconciliation, performs an award versus budget review, confirms payroll expenses, reviews cost transfers, reviews interdepartmental transfers, and reviews/documents questionable GL accounts. The project grant manager submits all monthly reconciliations to the PI for oversight and approval.

4.2 Review and Approval of Responses to Solicitations

Not applicable.

4.3 Quality of Procured Items

All items purchased, as well as laboratory services contracted are carefully researched and negotiated. All contracts are reviewed annually for quality and competitiveness.

5 Documents and Records

All staff receive copies of the SCEDDBO Comprehensive QMP. The Comprehensive QMP is also posted on the SCEDDBO internal website for easy access. The database of human subjects and animal protocol training is maintained by Ms. Patricia McMillan and is posted to the SCEDDBO internal website for ready reference.

Procedures for the handling and custody of data are designed to ensure confidentiality and data integrity. All data collected are stored in an ACCESS database specifically designed to interface with the GIS spatial databases to be employed in the analyses. Data are stored on password-protected computers in locked offices. The computers and electronic network that support this project constitute a self-standing network without external access, are fully compliant with the Health Insurance Portability and Accountability Act, and thus ensure data confidentiality.

All paper files related to the data are shredded before disposal. All deleted electronic files are destroyed using the Eraser software program. Eraser completely removes files from hard disks. Unlike a standard delete, which only removes references to file locations, Eraser overwrites each file several times, clears cluster allocations and scrambles dates of file creation and modification. This process removes all traces of the files and ensures that sensitive data cannot be recovered.

5.1.1 Research Project A: Mapping Disparities in Birth Outcomes

Detailed recordkeeping of all datasets and spatial data layers generated under Project A is maintained on the private computer network where the data is stored. Descriptions of all original variables and related appendices associated with the Detailed Birth Record were provided by the North Carolina State Center for Health Statistics and are stored electronically with the data files. Metadata is requested on all environmental and socioeconomic datasets, and copies of all relevant correspondence with data sources are filed. Records are kept describing the steps necessary to prepare data for analysis and linkage with other datasets, including cleaning miscoded entries, creating specialized standard variables, and georeferencing addresses. Original copies of all datasets are backed up along with the code associated with each processing step.

Strategies for ensuring the traceability of data and the accuracy of analysis have been established and conveyed to all personnel working under Project A. New files are generated under a strict file structure and naming convention designed to facilitate data management. Metadata describing original data sources, spatial extent, projection, and spatial referencing techniques is produced with all spatial data layers. All geocoded address layers include additional documentation providing greater detail on the spatial reference layers and standardizations required in the geocoding process. The results of all statistical analysis comply with a template that includes details on data sources, data restrictions, final sample size, date produced, and the programmer.

5.1.2 *Research Project B: Healthy Pregnancy, Healthy Baby: Studying Racial Disparities in Birth Outcomes*

Participants in Research Project B are asked to complete a battery of eleven psychosocial surveys which are marked with the participant's unique identification number. Unfinished surveys are kept in an active folder which is taken to the participant's subsequent obstetrician visits. As surveys are finished, they are transferred to the participant's permanent file, marked as completed and entered into the data set. Survey data is entered as it is completed so any inconsistencies or ambiguities can be ascertained and clarified if necessary. Participant files are kept securely in filing cabinet in a locked office. All electronic data collected are stored in a Microsoft ACCESS database. Data are stored on password-protected computers in locked offices. The computers and electronic network that support this project constitute a self-standing network without external access, are fully compliant with the Health Insurance Portability and Accountability Act, and thus ensure participant confidentiality.

For Research Project B, bloods for genetic and proteomic analysis are drawn at 28 weeks when the participant has her glucola test. All identifying information is removed from the samples. Samples are assigned a Center for Human Genetics (CHG) acquisition number to maintain confidentiality. Blood is signed into the CHG server and taken to the CHG laboratory. Blood is then processed and frozen for future genetic analyses.

In addition, environmental blood draws are performed at delivery. The blood is then processed to remove all identifying information before being sent to the Duke Referral Laboratories at Duke University Health System. The Lab then sends the blood samples to the Mayo Clinic for analysis. Each blood sample has an identifying Mayo requisition number which corresponds to the identifying information which is housed in SCEDDBO's secure data base. Environmental reports are sent to SCEDDBO, using only the Mayo requisition number. The environmental results are then placed in the participant's folder. A document reporting the environmental results is prepared and reviewed by the Center PI and then mailed to the participant. A copy of the environmental report is also placed in the participant's folder.

5.1.3 *Research Project C: Perinatal Environmental Exposure Disparity and Neonatal Respiratory Health*

Morphologic measurements using image analysis are audited by a second team member to verify concordance and accuracy of measurements. The physiologic studies are directly overseen by the co-investigators during data acquisition in order to ensure that the measurements have been correctly obtained. Data entry is backed up using electronic forms, and data analysis is performed using coded group identifications to maintain masking of treatment assignment.

5.1.4 *GISSA Facility Core*

In its function as a central repository for the data collected and produced by the individual projects, the GISSA Core provides data management across projects to ensure data confidentiality and integrity. Data is housed on a private network designed to both ensure data confidentiality and facilitate access to data for investigators in all projects. Confidentiality of data is protected by an electronic network that is fully compliant with the Health Insurance Portability and Accountability Act. The file structure in place on this network was constructed to store data files in such a way that personnel with appropriate permissions can easily locate datasets of interest, along with all relevant documentation needed to use the data accurately.

All data handled by the GISSA Core is subject to strict conventions designed to protect data integrity and traceability. Proper documentation is required for all datasets submitted to the GISSA Core by individual projects or received from external data sharing partners. At a minimum, this documentation includes source and contact information, collection method and completeness, variable coding definitions, confidentiality requirements, and date received by the Core. In addition to the documentation required for all datasets, spatial layers also include metadata describing geographic extent, projection, and georeferencing techniques. As new files are provided or generated, they are stored on the private network within the file structure and naming conventions established by the GISSA Core to facilitate data management. Traceability and accuracy of statistical analysis is ensured by requiring all output include a coversheet detailing data sources, data restrictions, final sample size, date produced, programmer name, and software package used.

6 Computer Hardware and Software

SCEDDBO's data manager develops, installs, tests, maintains, controls, and documents computer hardware and software used in SCEDDBO projects. The data manager also evaluates purchased hardware and software to ensure it meets user requirements and complies with applicable contractual requirements and standards. The data and information produced from or collected by computers will meet applicable information resource management requirements and standards.

7 Planning

7.1 Planning Environmental Data Operations

For each of the three research projects, a detailed plan for data collection has already been developed. These plans were described in the SCEDDBO research application to the EPA and are summarized below. Each of the plans has been piloted and revised as needed. All plans are fully operational at this point.

7.1.1 Research Project A: Mapping Disparities in Birth Outcomes

Data are obtained from existing medical/health databases, such as the North Carolina detailed birth record and the Duke Obstetrical Tracevue database, as well as publicly available information such as U.S. Census Data, Toxic Release Inventory (TRI), and County Tax Assessments.

All data collected are stored in an ACCESS database specifically designed to interface with the GIS spatial databases to be employed in the analyses. Data are stored on password-protected computers in locked offices. The computers and electronic network that support this project constitute a self-standing network without external access, are fully compliant with the Health Insurance Portability and Accountability Act, and thus ensure data confidentiality. Use of the detailed birth record data is also governed by a data sharing agreement between the North Carolina State Center for Health Statistics and Duke's Children's Environmental Health Initiative.

Except when required by law, subjects in the medical/health databases are not identified by name, social security number, address, telephone number, or any other direct personal identifier in study records disclosed outside of the SCEDDBO private data server environment.

7.1.2 *Research Project B: Healthy Pregnancy, Healthy Baby: Studying Racial Disparities in Birth Outcomes*

There are two types of research material in the proposed study: 1) blood samples to be analyzed for neuroendocrine and inflammatory proteins, environmental toxins, and genotyping; and 2) responses to questionnaires assessing personality dimensions and other psychosocial characteristics. These are obtained from individually identifiable living human beings. The material and data being obtained is specifically for research purposes.

Procedures for the handling and custody of samples are designed to ensure patient confidentiality and data integrity. Consent for collection and use of clinical data and biologic samples is obtained in accordance with the Duke IRB-approved protocol #7227-07-5ER. Consent for use of biologic samples within the CHG DNABank Repository is obtained in accordance with the Duke IRB-approved protocol 0699-05-4R5DB. At approximately 24 – 28 weeks gestation, subjects undergo venipuncture to obtain 20-25 mL of blood for DNA analyses and measurement of neuroendicrine and inflammatory proteins. If the subject is scheduled for routine clinical laboratory studies, then study samples are obtained at the same time in the outpatient laboratory, which is located adjacent to the outpatient OB/GYN clinics at both study sites. Upon admission to Labor and Delivery, another 20-25 mL of blood are obtained at the time of peripheral intravenous catheter placement or at the time of a routine clinical laboratory study for environmental exposure studies. If either sample cannot be obtained at the time of a routine clinical study, venipuncture is performed and samples are collected by trained research personnel.

Extensive efforts are made by the CHG DNA Bank to ensure confidentiality of all subjects (CHG DNABank Repository, Registry# 0699-05-4R5DB). All research samples accepted by the DNA Bank are assigned a consecutive sample number. Identifying information provided on the sample is replaced by a computer-generated barcoded label and the links are retained in the PEDIGENE® database. Identifying information in PEDIGENE® is restricted to principal investigators and designated clinical assistants for only the IRB-approved studies they work on, and computer personnel. Access to the PEDIGENE® database requires a password from the CHG database administrator. Passwords are issued only with the approval of a faculty member or the PI of an IRB-approved study using the DNA Bank samples, and only for the specific IRB-approved research studies to which the user needs access. Authorizations are reviewed monthly, and passwords are changed every 180 days. All data modification activity is logged, including the identity of the individual on the system. All allocation and research procedures are performed by sample number only. Repository records that identify subjects are kept confidential as required by law. Federal Privacy Regulations provide safeguards for privacy, security, and authorized access. Except when required by law, subjects are not identified by name, social security number, address, telephone number, or any other direct personal identifier in study records disclosed outside of the SCEDDBO private data server environment.

Samples stored at the CHG DNA Bank designated for protein analyses are sent in batches to the Proteomics Core facility. Federal Privacy Regulations provide safeguards for privacy, security, and authorized access. All samples are labeled only with the unique study identification number assigned to each individual participant at the time of study enrollment. Except when required by law, subjects are not identified by name, social security number, address, telephone number, or any other direct personal identifier in study records disclosed outside of the SCEDDBO private data server environment.

Samples obtained at the time of delivery for environmental analyses are processed by the Duke Referral Laboratories and subsequently sent to the Mayo Clinical Laboratories in Rochester, Minnesota. Federal Privacy Regulations provide safeguards for privacy, security, and authorized access. All samples and requisition forms are labeled only with the unique study identification number assigned to each individual participant at the time of study enrollment. Except when required by law, subjects are not identified by name, social security number, address, telephone number, or any other direct personal identifier in study records disclosed outside of the SCEDDBO private data server environment. Results of environmental assays are reported directly to SCEDDBO research staff and not to the Duke Referral Laboratories. All results are maintained as part of the research protocol and not entered into a participant's medical record. Results are conveyed to study participants via an environmental sampling report.

All data collected are stored in a Microsoft ACCESS database. Data are stored on password-protected computers in locked offices. The computers and electronic network located within the Nicholas School of the Environment constitute a self-standing network without external access, are fully compliant with the Health Insurance Portability and Accountability Act, and thus ensure participant confidentiality.

7.1.3 Research Project C: Perinatal Environmental Exposure Disparity and Neonatal Respiratory Health

Procedures for the handling and custody of samples are designed to ensure appropriate treatment assignment masking and data integrity. Samples are stored in refrigerators or freezers that are on monitored alarms and backup emergency power.

All major laboratory instrumentation, as well as balances and freezers, are routinely examined by authorized service personnel to insure proper function. All chemical and biochemical assays used in our laboratory are based upon published methodologies. Detailed protocols are maintained in laboratory notebooks, and deviations in these protocols from published procedures are carefully noted.

Numerous routine measures are taken to insure the precision and accuracy of our data, the appropriateness of statistical data analyses and interpretation, and the secure maintenance of data records.

This study design and associated analytical methods have been extensively reviewed by several scientists. In addition, the Science Advisory Committee will provide regular evaluation of the direction and progress of the work. Manuscripts generated from this project will be submitted for peer-reviewed publication, and thus the quality and success of the research will be independently evaluated by experts in the field.

7.1.4 GISSA Facility Core

In addition to its function as a central data repository (described above), the GISSA Facility Core provides extensive analytical support on general statistical, spatial statistical, and genetic analysis. All hardware and software used to undertake the analysis is extensively reviewed before adoption. In addition, analytical code is often written *de novo*. This code is reviewed by multiple staff members to assure that it is correct. Data quality checks are routinely incorporated into the daily operations of the GISSA Facility Core (see above).

8 Implementation of Work Processes

All work is performed according to our existing research protocols. Activities under each project and facility core are discussed during monthly Internal Steering Committee meetings to assess compliance with research protocol and QA documents. Should changes be required, these will be discussed during the Internal Steering Committee meetings. Any changes will be reflected in revised research protocols and will be communicated to all staff associated with the affected project or facility core. The QA Manager, Dr. Pamela Maxson, will confirm with each staff member of the relevant SCEDDBO component that they are: 1) aware of the changes; and 2) understand the implications of the changes for daily research operations.

9 Assessment and Response

The QA Manager, Dr. Pamela Maxson, and the liaison people from each individual research project will prepare a concise document annually on compliance by each respective research project and facility core with the SCEDDBO Comprehensive Quality Management Plan. This document will be discussed and reviewed at one of the twice-yearly SCEDDBO research retreats. Any concerns or issues raised will be discussed and hopefully resolved at this stage. If not, the conflict will enter dispute resolution involving Dr. Maxson, the respective liaison, and the involved parties. If necessary, SCEDDBO Principal Investigator/Director, Dr. Marie Lynn Miranda, will be the ultimate decision maker regarding the issue.

10 Quality Improvement

All staff members will have access to the Quality Assurance Manager to discuss any Quality Assurance concerns. In addition, there is a mechanism for anonymous reporting of concerns if necessary. In addition, quality improvement will be assured through monthly SCEDDBO meetings.

SCEDDBO Principal Investigator/Director, Dr. Marie Lynn Miranda, and Quality Assurance Manager, Dr. Pamela Maxson, will attend one of each of the research project team meetings every quarter to discuss QA concerns and garner feedback and input.

Particularly for Research Project B, there is a toll free number staffed bilingually for all study participants to ensure they can ask any questions that come up regarding their participation in the study. Any Quality Assurance issue raised through this mechanism will be discussed at Internal Steering Committee meetings. It is of primary importance to SCEDDBO that human subjects are treated in accordance with human subjects' criteria.

QUALITY ASSURANCE REVIEW FORM
(Extramural Assistance Agreements and Interagency Agreements)

I. GENERAL INFORMATION

Descriptive Title: Southern Center for Environmentally-Driven Disparities in Birth Outcomes

Principal Investigator: Marie Lynn Miranda

Program Office:	NCER, ORD	
Approximate Amount:	Total Project Funding:	$ 7,735,620
	Total EPA Budget:	$ 7,735,620
Budget & Project Periods:	5 Years	

II. DESCRIPTION OF WORK

	YES	NO
This agreement involves data that describe environmental processes or conditions; ecological or health effects and consequences; the performance of environmental technology (whether hardware-based or via new techniques); or the use of survey, models or secondary data. If yes, complete section III.	X	

III. QUALITY ASSURANCE ASSISTANCE AGREEMENT REQUIREMENTS

		YES	NO
1.	The proposal QA statement is satisfactory for award considering the extent of environmental data collection activities.	X	
2.	A more detailed statement (i.e., Quality Management Project Plan (QMPP)) is also required as a condition of the agreement.		X
3.	Discussions of QA/QC issues are required as a part of the progress reports and/or final report. (N/A for conference support)	X	
4.	During any evaluation of the progress of the agreement (such as an on-site review), the PO will determine if the QA system is operational and exhibits the capability for successful completion of this project.	X	

The signatures below verify that the QA requirements have been established prior to award.

Project Officer:	QA Officer Concurrence: Holly Ferguson
Nigel Fields	
Signed electronically via funding recommendation approvals.	**Signed electronically via funding recommendation approvals.**